Remarks

The Examiner asserts that there is insufficient support in the description for the general term "paralyzing agent". The Applicant maintains that at several points in the description, there is support for this term (e.g. paragraph 1 - "a paralyzing agent"; paragraph 32 - "or its equivalent"; paragraph 42 – "agents, other than botulinum toxin, may be used to relax the intrinsic muscles"; paragraph 46 – "a paralyzing agent"). However, to expedite allowance of the present application, claim 9 and has been amended to replace the term "paralyzing agent" with the term "botulinum toxin" and claim 23 has been deleted. Claim 24 has been amended to refer to "botulinum toxin" and to depend from claim 9. The Applicant maintains the right to pursue the original claims in a continuation application. New claim 30 has been added to specifically claim one preferred embodiment in which the muscles are pretreated with an acupuncture needle to release the spinal scar.

Claims 9 and 21-27 are rejected as obvious in view of Donovan, Aoki, Share and Borodic. The present claims are directed to methods of treating **spinal compression** which comprise administering botulinum toxin to the **intrinsic muscles**. The present invention is useful not only to treat pain but also to promote healing of vertebral discs by alleviating the pressure caused by spinal spasm or scarring. The present invention provides pain relief by treating the cause of the pain (i.e. spinal compression). The intrinsic muscles which are the target of the treatment are a specific set of deep spinal muscles as described in paragraph 32 of the present application. The present claims specify that the toxin is administered to the intrinsic muscles not just any spinal muscle. Since these muscles are very small and sometimes difficult to reach, the type of treatment described in the present application had not previously been attempted.

Donovan, on the other hand, uses botulinum toxin to treat pain, such as that associated with bone tumors, by administering a toxin derivative coupled to a targeting moiety. The targeting moiety is selected so that the agent targets neurons having receptors

for neurotransmitters that are released for the transmission of pain signals. In fact, at the bottom of column 12, Donovan teaches that it preferable to modify the toxin to **incapacitate** its ability to bind to receptors at the neuromuscular junction. In addition, At column 18, lines 1-5, the term "intraspinal" is defined as meaning the epidural space, the intrathecal space, the grey or white matter of the spinal cord or the dorsal root or dorsal root ganglion. There is no teaching or suggestion in Donovan that the toxin be applied to the intrinsic muscles to prevent them from contracting and causing spinal compression and Donovan actually teaches away from such an administration.

Aoki teaches a method for relieving pain associated with muscle contractions and provides at column 2, lines 53-64 a large number of conditions that can be treated using the method. At column 3, line 10 Akoi teaches that the use of the toxin in accordance with the present invention with regard to organ systems which involve the release of neurotransmitter. In example 2 (the only one at all related to the spine), spasmodic torticollis as manifested by contractions of the neck musculature is treated by administration of botulinum toxin but there is no teaching of how or where the toxin is administered. There is no mention in Akoi of treating spinal compression disorders such as disc herniation to promote healing and certainly no mention of an injection directly into the intrinsic muscles.

The Examiner asserts that from a combination of these two references it would be obvious to use the botulinum toxin to induce paralysis in any muscle that was causing pain. The Examiner also asserts that by further combining these two references with Borodic and Rasmussen, it would have been obvious to administer the toxin to the intrinsic muscles. Borodic discusses administration to paraspinal muscles such as the longissimus dorsi and the erector spinae. These are **extrinsic** muscles. The use is not directed to the treatment of a spinal compression disorder such as a herniated disc and there is no teaching of administration to the deep intrinsic muscles of the spine. As taught at page 4 of the present application, the intrinsic muscles are the deepest set of muscles

designed to provide structural integrity to the spine. The Rasmussen reference is an abstract with only vague allusions to treating spasticity in children. There is no teaching of treating a compression disorder by administering botulinum toxin to the intrinsic muscles.

It is respectfully submitted that none of the cited references either alone or in combination suggests injecting the toxin directly into the intrinsic muscles, not is there any suggestion to combine the treatments to come up with a treatment for spinal compression disorders. In the present invention, unlike the cited references, referred pain and dysfunction are reduced by indirect means of reducing vertebral and disk decompression. The present invention provides the surprising result that by preventing the intrinsic muscles from contracting, botulinum toxin is able to not only reduce the pain associated with spinal compression but also to prevent the compression from recurring for a time sufficient for the damaged tissue to heal. None of the cited references suggest that such an effect could be achieved and none of the cited references suggest that the intrinsic muscles could be injected. The intrinsic muscles are very small and sometimes difficult to reach so it would not be obvious to use them as a target for treatment. The Examiner is therefore asked to withdraw the rejection of claims 9 and 21-28 as obvious.

The Examiner also rejected claim 25 on the grounds that it would have been obvious to use the claimed dosages. It is respectfully submitted that, since no one else had injected the intrinsic muscles and these muscles are very small but also very strong, the required dosage would not have been obvious. In addition, it is known that different types of botulinum toxin are required in different amounts for different applications. Thus, selection of a dosage range requires experimentation and is not obvious.

Claims 26 and 27 are rejected as being obvious in view of the previously cited references further in view of Share et al. and Moyer et al. The Share et al. reference is not at all related to botulinum toxin and is directed to the use of a completely different agent to treat muscle spasm. The Moyer passage cited by the Examiner is a general discussion

of the effects of botulinum toxin, particularly botulinum toxin B. There is no suggestion in either of the references of an injection into the intrinsic muscles to paralyze the muscles and allow healing to occur. The use of single of plural injections is irrelevant since they are discussing an entirely different type of treatment. The Examiner is therefore asked to withdraw the objection.

The Examiner has rejected claim 28 as obvious in view of the above cited references with further regard to either of DeSimone and Ferree. DeSimone teaches a method of increasing IGF-1 for the therapeutic treatment of a variety of diseases included herniated discs. However, Desimone does not teach or suggest that the treatment can be enhanced by reducing the pressure on the herniated disc by preventing the intrinsic spinal muscles from contracting. It is therefore respectfully submitted that it would not be obvious to combine De Simone with the other references which do not teach paralysis of the intrinsic muscles to achieve the present invention.

In conclusion, none of the cited references teach injection of the intrinsic muscles. None of the cited references provide details of the injection methods. For example, the type of needle used is not specified. The intrinsic muscles are typically 2 ½ to 3 ½ inches below the skin and therefore a needle long enough to reach them is required. For botulinum injections for muscle paralysis, 27 gauge needles are typically used but they are only about one inch long and thus would not be able to reach the intrinsic muscles. Furthermore, none of the cited references suggest that injection of the intrinsic muscles may promote healing of injured tissue. Even a combination of all nine cited references would not lead one skilled in the art to the present invention.

In view of the above comments and the amendments to the claims, the Examiner is respectfully asked to withdraw the objections to the claims on the basis of obviousness.

Respectfully submitted,

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I hereby certify that this correspondence is being transmitted by facsimile to the U.S. Patent and Trademark Office, c/o Technology Center 1600, Attn: Examiner Zachariah Lucas, at facsimile number 703-872-9306 on October 30, 2003.

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